Article 34 Amendments

AMENDMENT

(pursuant to Article 11 of the [illegible]

To: Commissioner of the Patent Office

1. International Application Classification: PCT/JP04/004620

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4. Object of the Amendment:

(1) Specification

(2) Claims

5. Content of the Amendment

(1) The text "support matrix" on page 1, line 7 and page 3, line 24 of the specification is corrected to "cylindrical support matrix with a bellows-shaped section".

(2) The text "3. A composite according to aspect 2 of the invention, wherein the fiber structure is an aliphatic polyester." on page 3, line 27 of the specification is corrected to "3. (deleted)."

(3) The text "5. A composite according to aspect 1 of the invention, wherein the support matrix is a cylindrical body

with a bellows-shaped section." on page 4, line 3 of the specification is corrected to "5. (deleted)."

(4) The text "9. A composite according to aspect 8 of the invention, wherein the fiber structure is an aliphatic polyester." on page 4, line 12 of the specification is corrected to "9. (deleted)."

(5) The text "is preferably a cylindrical body" on page 5, line 24 of the specification is corrected to "is a cylindrical body".

(6) The text "support matrix" in claim 1, line 2 (page 1) is corrected to "cylindrical support matrix with a bellows-shaped section".

(7) Claims 3, 5 and 9 are deleted.

(8) The text "fiber structure" in claim 7, line 1 (page 1) is corrected to "fiber structure made of an aliphatic polyester".

6. List of Attached Documents

(1) Specification, page 1, page 1/1, page 3, page 4, page 5 (one sheet each)

(2) Claims, page 15, page 16 (one sheet each)

DESCRIPTION

COMPOSITE OF SUPPORT MATRIX AND COLLAGEN, AND METHOD FOR PRODUCTION OF SUPPORT MATRIX AND COMPOSITE

Technical Field

The present invention relates to a composite composed of collagen and a cylindrical support matrix with a bellows-shaped section made of a fiber structure composed of aliphatic polyester fibers with a mean fiber size of 0.05-50 μm, to a cylindrical support matrix having a bellows-shaped section, and to a method for production of the support matrix and a method for production of the composite.

Background Art

Recent years have seen an increase in active research in regenerative medicine, a technical field which takes advantage of the ability of cells to differentiate and proliferate to achieve reconstruction of original biological tissues and organs, as a method for treating major injury to or loss of biological tissue and organs. Neural regeneration is a branch of this field, and research is underway toward using tubes composed of artificial materials for crosslinking between stumps in the neuron-deficient sites of patients with ablated neural tissue, to induce regeneration of the neural tissue. Such tubes are made of silicon, polyurethane, polylactic acid, polyglycolic acid, polycaprolactone or their copolymers or composites, and they are often internally coated with collagen or laminin.

For vascular regeneration there are used artificial material tubes made of polytetrafluoroethylene, polyester, polylactic acid, polyglycolic acid, polycaprolactone or their copolymers or composites, and these are also often internally coated with gelatin, albumin, collagen or laminin.

For example, Japanese Unexamined Patent Publication HEI No. 6-285150 describes artificial vessels obtained by injecting insoluble collagen into the walls of cylindrical tubes made of a fibrous substance, and then subjecting them to chemical treatment before drying.

Also, Japanese Unexamined Patent Publication HEI No. 7-148243 discloses an implant material whose matrix is a biocompatible bulky structure comprising organic fibers in a three-dimensional woven texture or knitted texture, or a composite texture obtained as a combination thereof,

Since the aforementioned silicon, polyurethane, polytetrafluoroethylene and polyester materials lack bioabsorption properties, they are associated with problems from the standpoint of long-term safety, while compression and damage to regenerated nerves and vessels is also a concern. Also, polylactic acid, polyglycolic acid, polycaprolactone and their copolymers, while having bioabsorption properties, are problematic in terms of Young's modulus and stretchability, and can likewise lead to compression and damage to regenerated nerves and vessels. In other words, no tubes are known at the current time which exhibit superior performance from the standpoint of bioabsorption, Young's modulus and stretchability.

These problems can potentially be overcome by using composites of elastic materials such as collagen with support matrices made of polylactic acid, polyglycolic acid, polycaprolactone and their copolymers, but since conventionally known support matrices made of polylactic acid, polyglycolic acid, polycaprolactone and their copolymers lack stretchability, they counter the elastic property of the collagen and thus limit the use of such materials in the body. In other words, the currently known support matrices made of polylactic acid, polyglycolic acid, polycaprolactone and their copolymers, and composites of such support matrices with collagen, do not exhibit excellent stretchability.

Disclosure of the Invention

It is an object of the present invention to provide a matrix having high stretchability and an adequate Young's modulus (elastic modulus), as a tube which can serve as the matrix for an artificial vessel or for neural regeneration.

More specifically, the object is to provide such a matrix wherein the tube is a polymer compound having a bioabsorption property.

The aspects of the present invention are as follows.

1. A composite comprising collagen and a cylindrical support matrix with a bellows-shaped section made of a fiber structure composed of aliphatic polyester fibers with a mean fiber size of 0.05-50 μm.

2. A composite according to aspect 1 of the invention, wherein the fiber structure is a biodegradable polymer.

3. (deleted)

4. A composite according to aspect 1 of the invention, wherein the aliphatic polyester is polylactic acid, polyglycolic acid, polycaprolactone or a copolymer thereof.

5. (deleted)

6. A composite according to aspect 5 of the invention, wherein the cylindrical body is a cylindrical body which is composed of a fiber structure with a basis weight of 1-50 g/m^2 and has a membrane thickness of 0.05-0.2 mm and a diameter of 0.5-50 mm, wherein the spacing of the bellows-shaped section is no greater than 2 mm and the depth of the bellows-shaped section is 0.1-10 mm.

7. A cylindrical body characterized by being composed of a fiber structure with a basis weight of 1-50 g/m^2 and having a membrane thickness of 0.05-0.2 mm and a diameter of 0.5-50 mm, wherein the spacing of the bellows-shaped section is no greater than 2 mm and the depth of the bellows-shaped section is 0.1-10 mm.

8. A cylindrical body according to aspect 7 of the invention, wherein the cylindrical body is a biodegradable polymer.

9. (deleted)

10. A cylindrical body according to aspect 7 of the invention, wherein the aliphatic polyester is polylactic acid, polyglycolic acid, polycaprolactone or a copolymer thereof.

11. A cylindrical body according to aspect 7 of the invention, wherein the mean fiber size of the cylindrical body is 0.05-50 μm.

12. A method for production of a cylindrical body composed of a fiber structure with a basis weight of 1-50 g/m^2, wherein the spacing of the bellows-shaped section is no greater than 2 mm and the depth of the bellows-shaped section is 0.01-0.1 mm, which method comprises a stage of producing a solution of an aliphatic polyester in a volatile solvent, a stage of spinning the solution by an electrostatic spinning method, a stage of obtaining a fiber structure accumulated on a collector, and a stage of molding the fiber structure into a cylindrical body having a bellows-shaped section with a spacing of no greater than 2 mm.

13. A method for production of a composite composed of a cylindrical body and collagen, wherein a composite is formed of a cylindrical body produced by a method according to aspect 12 of the invention, and collagen.

14. A method for production of a composite composed of a cylindrical body and collagen, wherein a cylindrical body produced by a method according to aspect 12 of the invention is impregnated with a solution comprising collagen dissolved and/or dispersed in a solvent, and then at least one method is employed to fix the collagen by gelling, crosslinking or drying.

Brief Explanation of the Drawings

Fig. 1 is an example of an apparatus used in an electrostatic spinning method wherein the spinning solution is discharged into an electrostatic field, as a production method of the invention.

Fig. 2 is an example of an apparatus used in an electrostatic spinning method wherein fine droplets of the spinning solution are introduced into an electrostatic field, as a production method of the invention.

Fig. 3 is a cross-sectional view of a cylindrical body according to the invention.

Best Mode for Carrying Out the Invention

The present invention will now be explained in greater detail. The examples and explanation which follows are only illustrative of the invention and, needless to mention, modifications may be implemented which are within the scope of the invention.

The fiber structure used for the invention may be a three-dimensional structure formed by laminating and accumulating single or multiple filaments. The form of the structure may be, for example, a nonwoven fabric, woven fabric, knitted fabric, mesh, yarn or the like.

The composite used for the invention is a composite composed of the aforementioned fiber structure and collagen.

The fiber structure used for the invention is made of an aliphatic polyester.

As aliphatic polyesters there may be mentioned polylactic acid, polyglycolic acid, lactic acid-glycolic acid copolymer, polycaprolactone, polybutylene succinate, polyethylene succinate and their copolymers. Preferred aliphatic polyesters among these are polylactic acid, polyglycolic acid, lactic acid-glycolic acid copolymer and polycaprolactone, with polylactic acid and polycaprolactone being particularly preferred.

The fiber structure used for the invention is a cylindrical body with a bellows-shaped section.

The fiber structure of the invention has a basis weight of 1-50 g/m^2, and is preferably not less than 1 g/m^2 because a structure will not be satisfactorily formed. It is also preferably not greater than 50 g/m^2 because...

CLAIMS

1. (amended) A composite comprising collagen and a cylindrical support matrix with a bellows-shaped section made of a fiber structure composed of aliphatic polyester fibers with a mean fiber size of 0.05-50 μm.

2. A composite according to claim 1, wherein said fiber structure is a biodegradable polymer.

3. (deleted)

4. (amended) A composite according to claim 1, wherein said aliphatic polyester is polylactic acid, polyglycolic acid, polycaprolactone or a copolymer thereof.

5. (deleted)

6. (amended) A composite according to claim 1, wherein said cylindrical body is a cylindrical body which is composed of a fiber structure with a basis weight of 1-50 g/m^2 and has a membrane thickness of 0.05-0.2 mm and a diameter of 0.5-50 mm, wherein the spacing of the bellows-shaped section is no greater than 2 mm and the depth of the bellows-shaped section is 0.1-10 mm.

7. (amended) A cylindrical body characterized by being composed of a fiber structure made of an aliphatic polyester, with a basis weight of 1-50 g/m^2 and having a membrane thickness of 0.05-0.2 mm and a diameter of 0.5-50 mm, wherein the spacing of the bellows-shaped section is no greater than 2 mm and the depth of the bellows-shaped section is 0.1-10 mm.

8. A cylindrical body according to claim 7, wherein said cylindrical body is a biodegradable polymer.

9. (deleted)

10. A cylindrical body according to claim 7, wherein said aliphatic polyester is polylactic acid, polyglycolic acid, polycaprolactone or a copolymer thereof.

11. A cylindrical body according to claim 7, wherein the mean fiber size of said cylindrical body is 0.05-50 μm.

12. A method for production of a cylindrical body composed of a fiber structure with a basis weight of 1-50 g/m^2, wherein the spacing of the bellows-shaped section is no greater than 2 mm and the depth of the bellows-shaped section is 0.01-0.1 mm, which method comprises a stage of producing a solution of an aliphatic polyester in a volatile solvent, a stage of spinning said solution by an electrostatic spinning method, a stage of obtaining a fiber structure accumulated on a collector, and a stage of molding said fiber structure into a cylindrical body having a bellows-shaped section with a spacing of no greater than 2 mm.

13. A method for production of a composite composed of a cylindrical body and collagen, wherein a composite is formed of a cylindrical body produced by a method according to claim 12, and collagen.

14. A method for production of a composite composed of a cylindrical body and collagen, wherein a cylindrical body produced by a method according to claim 12 is impregnated with a solution comprising collagen dissolved and/or dispersed in a solvent, and then at least one method is employed to fix the collagen by gelling, crosslinking or drying.